29. (New) The method of treating T-cell mediated disease or infection of any of claims 27 or 28, wherein the *Notch*-ligand is selected from Serrate, Delta or fragments, derivatives or analogs thereof.

30. (New) A method of affecting linked suppression comprising administering a *Notch*-ligand, or fragments, derivatives or analogs thereof, to a patient in need thereof.

31. (New) A method of affecting infectious tolerance comprising administering a *Notch*-ligand, or fragments, derivatives or analogs thereof, to a patient in need thereof.

32. (New) A method of modulating expression of a functional *Notch*-protein or *Notch* signaling pathways involving a *Notch*-ligand. --

---

REMARKS

Reconsideration and withdrawal of the requirement for restriction are respectfully requested in view of the amendments, and remarks herewith, which place the application in condition for allowance.

I. STATUS OF CLAIMS

Claims 1-32 are now pending. Claims 1-4 and 23 are amended. New claims 27-32 are added.

No new matter is added by these amendments.

Claims 1-4 and 23 are amended, and new claims 27-32 are added, to better define and more distinctly claim the instant invention. Claims 1-4 are amended to replace the "use" language with "method" in order to conform with settled U.S. practice. Claim 23 is rewritten in independent form. Support for the amended recitations in claims 1-4 and 23 are found in the original claims and throughout the specification. Support for new claims 27-32 are found in original claims 2-6 and 26, respectively.

II. RESPONSE TO RESTRICTION REQUIREMENT

The October 3, 2000 Office Action required an election under 35 U.S.C. § 121 from:

Group I. Claims 1-6, 13-17 and 26, drawn to *Notch* ligand, classified in class 530, subclass 350.

Group II. Claims 7-12, drawn to a method of tolerizing T cells to an antigen or allergen using *Notch*-ligand expressing antigen presenting cells (APCs), classified in class 435, subclass 373.

Group III. Claim 18, drawn to a kit comprising *Notch* protein or family members, classified in class 530, subclass 350 and class 435, subclass 810.

Group IV. Claim 19, drawn to an assay determining the effect of a compound on ligand binding to *Notch*, classified in class 436, subclass 501.

Group V. Claim 20, drawn to *Delta* or *Serrate* ligand, classified in class 530, subclass 350.

Group VI. Claim 21, drawn to an assay for free *Serrate*, *Notch* or *Delta* family members in vivo, classified in class 424, subclass 9.1.

Group VII. Claim 22, drawn to an assay for determining a compound's effect on *Notch* or ligand expression, classified in class 435, subclass 6.

Group VIII. Claim 23, drawn to compounds which affect *Notch* or ligand expression, classified in class 536, subclass 24.5.

Group IX. Claims 24 and 25, drawn to a compound which downregulates *Delta* or *Serrate* expression, classified in class 536, subclass 24.5.

Applicants provisionally elect, with traverse, for further prosecution in this application, the invention of Group I, claims 1-6, 13-17 and 26, drawn to *Notch* ligand, classified in class 530, subclass 350. Reconsideration and withdrawal of the restriction requirement are respectfully requested in view of the remarks herewith.

The *Notch* receptor family and its ligands, *Delta* and *Serrate*, are expressed on the cell surface of normal adult cells of the peripheral immune system. Consequently, the present invention relates to the use of therapeutic compounds in the modification of T-cell activation. In particular, the invention relates to the use of therapeutic compounds in modulating the interaction between *Notch* protein family members and their *Delta* and *Serrate* ligands. The invention also relates to the therapeutic use of such compounds to treat, for example, graft rejection, autoimmunity, allergy, asthma, infectious diseases and tumors.

The present claims, therefore, represent a web of knowledge and continuity of

effort that merits examination in a single application. Indeed, the claims of Groups I, III and V are related since the claims of all three groups are classified in class 530, subclass 350. The claims of Group I and II are related as the claims of Group II are a subset of the method claims of Group I. The claims of Group I and VIII are related since claim 23 of Group VIII is a Group I product detected by a particular assay. The claims of Groups II, III and VII are related since the claims in all three groups are classified in class 435. The claims of Groups VIII and IX are related since the claims in both groups are classified in class 536, subclass 24.5. Finally, the claims of Groups IV and VI, although arguably classified in different classes, relate to assays involving *Notch* or its *Serrate* or *Delta* ligands. Indeed, all the claims are directed to the *Notch* receptor family and its *Delta* and *Serrate* ligands.

In this regard, the Examiner's attention is respectfully requested to review MPEP § 808.02 which states, ". . . even with patently distinct inventions, restriction is not (emphasis added) required unless one of the following reasons appears:

1. Separate classification;
2. Separate status in the art; or
3. Different field of search . . ."

Contrary to the guideline mandated by the MPEP, Groups I, III and V; Groups II, III and VII; and Groups VIII and IX are, respectively, in the same classes. Further, Groups IV and VI involve the same status in the art. Importantly, the claims in all nine Groups involve *Notch* or its *Delta* or *Serrate* ligands, thereby encompassing the same field of search. As an example, amended claim 23 in Group VIII is a Group I product detected by a particular assay

and should, consequently, be searched concurrently with the claims of Group I. Thus, restriction is not appropriate.

Additionally, the Examiner's attention is further respectfully invited to review the text of MPEP § 803 which in part states:

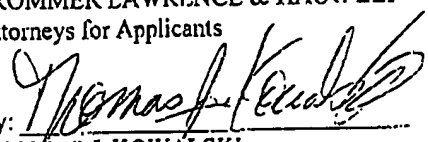
> If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions (emphasis added).

The result of the present restriction requirement are inefficiencies and unnecessary expenditures by both the Applicants and the PTO and extreme prejudice to Applicants (particularly in view of GATT, a shortened patent term may result in any divisional applications filed); and restriction has not been shown to be proper, especially since the requisite showing of serious burden has not been made in the Office Action and there are relationships between the claims of all nine Groups. Indeed, the search and examination of each Group is likely to be co-extensive and, in any event, would involve such interrelated art that the search and examination of the entire application can be made without undue burden on the Examiner. All of the preceding, therefore, mitigate against restriction.

In view of the foregoing, reconsideration and withdrawal of the restriction requirement and favorable examination of Claims 1 through 32 on the merits are respectfully requested.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: 
THOMAS J. KOWALSKI
Reg. No. 32,147

SAMUEL H. MEGERDITCHIAN
Reg. No. 45,678
(212) 588-0800